

IN THE CLAIMS:

Cancel claims 1-91, and add the following new claims:

92. An exendin derivative having an amino acid sequence that differs from the amino acid sequence of exendin-3 or exendin-4 by the substitution of up to ten amino acid residues with any α -amino acid residue, wherein (a) one or two lipophilic substituents are attached to amino acid residues and (b) one of the lipophilic substituents is attached to an amino acid residue which is not the N-terminal or C-terminal amino acid residue.
93. An exendin derivative of claim 92, having an amino acid sequence that differs from the amino acid sequence of exendin-3 or exendin-4 by the substitution of up to six amino acid residues with any α -amino acid residue.
94. An exendin derivative of claim 93, wherein one lipophilic substituent is present.
95. An exendin derivative of claim 93, wherein two lipophilic substituents are present.
96. An exendin derivative of claim 94, wherein the lipophilic substituent has 4 to 40 carbon atoms.
97. An exendin derivative of claim 96, wherein the lipophilic substituent has 8 to 25 carbon atoms.
98. An exendin derivative of claim 96, wherein the lipophilic substituent is attached by means of a spacer.
99. An exendin derivative of claim 98, wherein the spacer is an unbranched alkane α,ω -dicarboxylic acid group having from 1 to 7 methylene groups.
100. An exendin derivative of claim 99, wherein the spacer is an unbranched alkane α,ω -dicarboxylic acid group having two methylene groups.
101. An exendin derivative of claim 98, wherein the spacer is an amino acid residue except cys, or a dipeptide such as gly-lys.
102. An exendin derivative of claim 96, wherein the lipophilic substituent is a partially or completely hydrogenated cyclopentanophenathrene skeleton.

103. An exendin derivative of claim 96, wherein the lipophilic substituent is a straight-chain or branched alkyl group.

104. An exendin derivative of claim 96, wherein the lipophilic substituent is a straight-chain or branched acyl group.

105. An exendin derivative of claim 104, wherein the acyl group is of the formula $\text{CH}_3(\text{CH}_2)_n\text{CO}-$, wherein n is 4 to 38.

106. An exendin derivative of claim 105, wherein the acyl group is $\text{CH}_3(\text{CH}_2)_6\text{CO}-$, $\text{CH}_3(\text{CH}_2)_8\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{10}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{12}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{14}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{16}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{18}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{20}\text{CO}-$ or $\text{CH}_3(\text{CH}_2)_{22}\text{CO}-$.

107. An exendin derivative of claim 96, wherein the lipophilic substituent is an acyl group of a straight-chain or branched alkane α,ω -dicarboxylic acid.

108. An exendin derivative of claim 107, wherein the acyl group is of the formula $\text{HOOC}(\text{CH}_2)_m\text{CO}-$, wherein m is from 4 to 38.

109. An exendin derivative of claim 108, wherein the acyl group is $\text{HOOC}(\text{CH}_2)_{14}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{16}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{18}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{20}\text{CO}-$ or $\text{HOOC}(\text{CH}_2)_{22}\text{CO}-$.

110. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_p((\text{CH}_2)_q\text{COOH})\text{CHNH-CO}(\text{CH}_2)_2\text{CO}-$, wherein p and q are integers and p+q is an integer of from 8 to 33.

111. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_r\text{CO-NHCH}(\text{COOH})(\text{CH}_2)_2\text{CO}-$, wherein r is an integer of from 10 to 24.

112. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_s\text{CO-NHCH}((\text{CH}_2)_2\text{COOH})\text{CO}-$, wherein s is an integer of from 8 to 24.

113. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH-CO}(\text{CH}_2)_u\text{CH}_3$, wherein u is an integer of from 8 to 18.

114. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-COCH((CH}_2)_2\text{COOH)NH-CO(CH}_2)_w\text{CH}_3$, wherein w is an integer of from 10 to 16.

115. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-CO(CH}_2)_2\text{CH(COOH)NH-CO(CH}_2)_x\text{CH}_3$, wherein x is an integer of from 10 to 16.

116. An exendin derivative of claim 96, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-CO(CH}_2)_2\text{CH(COOH)NH-CO(CH}_2)_y\text{CH}_3$, wherein y is zero or an integer of from 1 to 22.

117. An exendin derivative of claim 97, having an amino acid sequence of HGEFTFTSDLKQMEEEEAVRLFIEWLKNGGX, wherein X = P or Y, or a fragment or an analogue thereof.

118. An exendin derivative of claim 97, having an amino acid sequence of HX1X2GTFITSDLKQMEEEEAVRLFIEWLKNGGPSSGAPPPS, wherein X1X2 = SD or GE, or a fragment or an analogue thereof.

119. An exendin derivative of claim 97, having an amino acid sequence of DLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPS, or a fragment or an analogue thereof.

120. An exendin derivative of claim 92, which is Arg¹⁸, Leu²⁰, Gln³⁴, Lys³³ (N^ε-(γ-aminobutyroyl(N^α-hexadecanoyl))) Exendin-4-(7-45)-NH₂.

121. An exendin derivative of claim 92, which is Arg³³, Leu²⁰, Gln³⁴, Lys¹⁸ (N^ε-(γ-aminobutyroyl(N^α-hexadecanoyl))) Exendin-4-(7-45)-NH₂.

122. A pharmaceutical composition comprising an exendin derivative of claim 92 and a pharmaceutically acceptable vehicle or carrier.

123. A method of treating insulin dependent or non-insulin dependent diabetes mellitus in a patient in need of such a treatment, comprising administering to the patient a therapeutically effective amount of a exendin derivative of claim 92 and a pharmaceutically acceptable carrier.